

Claims

1. (Withdrawn) A method of preparing a stable formulation of an ACE inhibitor which comprises the steps of:
dispersing or dissolving a metal compound in an alcohol to form a metallic alcoholic dispersion;
mixing said ACE inhibitor into said metallic alcoholic dispersion; and
mixing until a clear solution is attained.
2. (Withdrawn) The method of claim 1 wherein said alcohol comprises ethanol and water.
3. (Withdrawn) The method of claim 1 wherein said ACE inhibitor is quinapril hydrochloride.
4. (Withdrawn) The method of claim 1 wherein said metal compound comprises sodium bicarbonate.
5. (Withdrawn) The method of claim 1 wherein said metal is an alkali metal.
6. (Withdrawn) The method of claim 1 wherein said metal is an alkali earth metal.
7. (Withdrawn) The method of claim 1 further comprising adding at least one excipient to said clear solution.
8. (Withdrawn) The method of claim 7 further comprising adding an antioxidant to said clear solution.
9. (Withdrawn) The method of claim 8 wherein said antioxidant is selected from the group consisting of butyl hydroxyl anisol, butyl hydroxyl toluene, maleic acid, and ascorbic acid.

10. (Withdrawn) The method of claim 7 wherein said excipient comprises microcrystalline cellulose, sodium starch glycolate, or combinations thereof.
11. (Withdrawn) A storage-stable and bio-stable formulation of ACE inhibitor comprising less than 5% by weight of hydrolytic breakdown products and having a bio/storage stability ratio of less than about 3.5.
12. (Withdrawn) The formulation of claim 11 wherein said bio/storage stability ratio is less than 2.
13. (Withdrawn) The formulation of claim 12 wherein said bio/storage stability ratio is less than 1.
14. (Withdrawn) The formulation of claim 11 wherein said ACE inhibitor comprises quinapril hydrochloride.
15. (Withdrawn) The formulation of claim 11 wherein said ACE inhibitor comprises enalapril maleate, quinapril hydrochloride, benazepril hydrochloride, moexipril hydrochloride, lisinopril hydrochloride, indopril hydrochloride, forsinopril sodium, or combinations thereof.
16. (Withdrawn) The formulation of claim 11 wherein said ACE inhibitor is stabilized in the presence of sodium bicarbonate.
17. (Withdrawn) A bio-stable pharmaceutical formulation of ACE inhibitor prepared in accordance with claim 1 comprising less than 11% by weight of hydrolytic breakdown product after incubation at 40°C and 75% relative humidity for 10 days and subsequent contact with water maintained at 37°C for 3 hours.

18. (Withdrawn) The formulation of claim 17 comprising less than 8% by weight of hydrolytic breakdown product.
19. (Withdrawn) The formulation of claim 18 comprising less than 5% by weight of hydrolytic breakdown product.
20. (Withdrawn) A bio-stable pharmaceutical formulation of ACE inhibitor prepared in accordance with claim 1 comprising less than 3.5% by weight of hydrolytic breakdown product wherein said ACE inhibitor is freshly prepared and after said freshly prepared ACE inhibitor is contacted with water maintained at 37°C for 3 hours.
21. (Withdrawn) The formulation of claim 20 comprising less than 2.5% by weight of hydrolytic breakdown product.
22. (Withdrawn) The formulation of claim 21 comprising less than 1.5% by weight of hydrolytic breakdown product.
23. (Withdrawn) A pharmaceutical preparation comprising a pharmaceutically acceptable formulation of quinapril hydrochloride substantially free of breakdown products, wherein said breakdown products comprise quinaprilat and quinapril-DKP.
24. (Withdrawn) The pharmaceutical preparation of claim 23 which contains less than 12.5% breakdown products by weight of said formulation after incubation at 60°C and 75% relative humidity for 10 days.
25. (Withdrawn) The pharmaceutical preparation of claim 24 which contains less than 6% breakdown products by weight of said formulation after incubation at 60°C and 75% relative humidity for 10 days.

26. (Withdrawn) The pharmaceutical preparation of claim 25 which contains less than 3% breakdown products by weight of said formulation after incubation at 60°C and 75% relative humidity for 10 days.
27. (Withdrawn) The pharmaceutical preparation of claim 26 which contains less than 1.5% breakdown products by weight of said formulation after incubation at 60°C and 75% relative humidity for 10 days.
28. (Withdrawn) The pharmaceutical preparation of claim 23 wherein said preparation is freshly prepared and which contains less than 3.5% quinaprilat by weight of said formulation after contact with water maintained at 37°C for 3 hours.
29. (Withdrawn) The pharmaceutical preparation of claim 28 which contains less than 2% by weight quinaprilat.
30. (Withdrawn) The pharmaceutical preparation of claim 29 which contains less than 1.5% by weight quinaprilat.
31. (Original) A method of treating a cardiovascular disorder comprising administering a storage-stable and bio-stable formulation of ACE inhibitor comprising less than 5% by weight of hydrolytic breakdown products and having a bio/storage stability ratio of less than about 3.5.

32. (Withdrawn) A method of preparing a stable formulation of quinapril hydrochloride which comprises the steps of:
dispersing or dissolving a sodium compound in an alcohol to form a metallic alcoholic dispersion;
mixing quinapril hydrochloride into said metallic alcoholic dispersion to form a metallic alcoholic and active ingredient dispersion;
mixing a thickening agent into said metallic alcoholic and active ingredient dispersion; and
mixing until a clear solution is attained.
33. (Withdrawn) The method of claim 32 wherein said thickening agent comprises polyvinylpyrrolidone, polyethylene glycol, polyvinyl alcohol, or combinations thereof.
34. (Withdrawn) The method of claim 32 wherein said alcohol comprises ethanol and water.
35. (Withdrawn) The method of claim 32 wherein said sodium compound comprises sodium bicarbonate.
36. (Withdrawn) The method of claim 32 further comprising adding an antioxidant to said clear solution.
37. (Withdrawn) The method of claim 36 wherein said antioxidant is butyl hydroxyl anisol, butyl hydroxyl toluene, maleic acid, ascorbic acid, or combinations thereof.
38. (Withdrawn) The method of claim 32 further comprising adding at least one excipient to said clear solution.
39. (Withdrawn) The method of claim 38 wherein said excipient comprises microcrystalline cellulose, sodium starch glycolate, or combinations thereof.

40. (Withdrawn) A storage-stable and bio-stable pharmaceutical preparation of quinapril hydrochloride prepared in accordance with claim 32.
41. (Withdrawn) The pharmaceutical preparation of claim 40 comprising less than 5% by weight quinaprilat and having a bio/storage stability ratio of less than about 3.5.
42. (Withdrawn) The pharmaceutical preparation of claim 41 wherein said bio/storage stability ratio is less than 2.
43. (Withdrawn) The pharmaceutical preparation of claim 42 wherein said bio/storage stability ratio is less than 1.
44. (Withdrawn) The pharmaceutical preparation of claim 40 which contains less than 12.5% breakdown products by weight of said formulation after incubation at 60°C and 75% relative humidity for 10 days.
45. (Withdrawn) The pharmaceutical preparation of claim 44 which contains less than 6% breakdown products by weight of said formulation after incubation at 60°C and 75% relative humidity for 10 days.
46. (Withdrawn) The pharmaceutical preparation of claim 45 which contains less than 3% breakdown products by weight of said formulation after incubation at 60°C and 75% relative humidity for 10 days.
47. (Withdrawn) The pharmaceutical preparation of claim 46 which contains less than 1.5% breakdown products by weight of said formulation after incubation at 60°C and 75% relative humidity for 10 days.

48. (Withdrawn) The pharmaceutical preparation of claim 40 wherein said preparation is freshly prepared and which contains less than 3.5% quinaprilat by weight of said formulation after contact with water maintained at 37°C for 3 hours.
49. (Withdrawn) The pharmaceutical preparation of claim 48 which contains less than 2.5% by weight quinaprilat.
50. (Withdrawn) The pharmaceutical preparation of claim 49 which contains less than 1.5% by weight quinaprilat.
51. (Withdrawn) The pharmaceutical preparation of claim 40 comprising less than 11% by weight quinaprilat after incubation at 40°C and 75% relative humidity for 10 days and subsequent contact with water maintained at 37°C for 3 hours.
52. (Withdrawn) The formulation of claim 51 comprising less than 8% by weight quinaprilat.
53. (Withdrawn) The formulation of claim 52 comprising less than 5% by weight quinaprilat.
54. (Original) A method of treating a cardiovascular disorder comprising administering quinapril hydrochloride comprising less than 5% by weight quinaprilat and having a bio/storage stability ratio of less than about 3.5.
55. (Withdrawn) A method of preparing a stable formulation of an ACE inhibitor which comprises the steps of:
dispersing or dissolving a metal compound in an alcohol to form a metallic alcoholic dispersion;
mixing said ACE inhibitor into said metallic alcoholic dispersion;
mixing until a clear solution is attained; and
adding a cellulosic excipient to said clear solution.

56. (Withdrawn) The method of claim 55 wherein said cellulosic excipient is microcrystalline cellulose, parenchymal cellulose, powdered cellulose, methyl cellulose, hydroxyethyl cellulose, hydroxypropyl cellulose, methylhydroxyethyl cellulose, methylhydroxypropyl cellulose, carboxymethyl cellulose, derivatives thereof, salts thereof, esters thereof, or combinations thereof.
57. (Withdrawn) The method of claim 55 further comprising adding a starch to said clear solution.
58. (Withdrawn) The method of claim 57 wherein said starch comprises sodium starch glycolate.
59. (Withdrawn) The method of claim 57 comprising dry mixing said second excipient and said cellulosic excipient prior to addition to said clear solution.
60. (Withdrawn) A pharmaceutical dosage form comprising an ACE inhibitor prepared by dispersing or dissolving a metal compound in an alcohol to form a metallic alcoholic dispersion; mixing said ACE inhibitor into said metallic alcoholic dispersion; mixing until a clear solution is attained; and adding a cellulosic excipient to said clear solution.
61. (Withdrawn) The pharmaceutical dosage form of claim 60 wherein said ACE inhibitor comprises quinapril hydrochloride.
62. (Withdrawn) The pharmaceutical dosage form of claim 60 which is substantially free of saccharides.
63. (Withdrawn) A formulation of quinapril which is substantially free of saccharide.

64. (Withdrawn) The formulation of claim 63 which is substantially free of breakdown products after 3 months at 40°C and 75% relative humidity, wherein said breakdown products comprise quinaprilat and quinapril-DKP.
65. (Withdrawn) The formulation of claim 64 which contains less than 3% quinaprilat by weight of said formulation.
66. (Withdrawn) The formulation of claim 65 which contains less than 1% quinaprilat by weight of said formulation.
67. (Withdrawn) The formulation of claim 64 which contains less than 1% quinapril-DKP by weight of said formulation.
68. (Withdrawn) The formulation of claim 65 which contains less than 0.5% quinapril-DKP by weight of said formulation.
69. (Withdrawn) A formulation of quinapril which is substantially free of saccharide and which contains less than 1 % quinaprilat by weight of said formulation and less than 0.5 % quinapril-DKLP by weight of said formulation after storage at 25°C and ambient humidity for 12 months.
70. (Currently Amended) A method of comprising administering the a formulation of quinapril which is substantially free of saccharide and which contains less than 1 % quinaprilat by weight of said formulation and less than 0.5 % quinapril-DKLP by weight of said formulation after storage at 25°C and ambient humidity for 12 monthsclaim 69.